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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,510	12/10/2004	Diane Marie Harvey	21023P	9955

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,510	HARVEY ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,18 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Election filed 1/29/07 in response to the Office Action of 1/18/07 is acknowledged and has been entered. Applicant elected group I with traverse.

The traversal is on the ground(s) that a search of group I claims would include a search of groups II, III, and VIII claims. Applicant requests reconsideration and withdrawal of the restriction requirement and/or regrouping of the claims, such as combining groups I-II and VIII. This is not found persuasive. These arguments have been considered but are not found persuasive as such arguments do not apply when restriction is required under 35 USC 121 and 372, as in the instantly filed application. Thus, when the Office considers international applications as an International Searching Authority, as an International Preliminary Examining Authority, and during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-19 were pending.

Claims 2, 5-17 were cancelled by Applicant.

Claims 1, 3, 4, 18, and 19 are pending and currently under consideration.

Specification

The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 89, in particular). Applicant is required to delete all embedded hyperlinks and/or other form of browser-executable codes. See MPEP § 608.01.

The specification is objected to on pages 87-89 for improper disclosure of polynucleotide sequences, as it fails to comply with the requirements of 37 CFR 1.821 through 1.825. This definition sets forth limits, in terms of numbers of amino acids and/or numbers of nucleotides, at or above which compliance with the sequence rules is required. Nucleotide and/or amino acid sequences as used in 37 CFR 1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. (see MPEP 2422). Proper correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-19 recite the limitation "The substantially purified polypeptide of claim 1...". There is insufficient antecedent basis for this limitation in the claim. Claim 1 recites "A purified polypeptide..."; however, claim 1 does not recite a *substantially* purified polypeptide.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3, 4, 18, and 19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 1, 3, 4, 18, and 19 are drawn to polypeptides comprising SEQ ID NO:2 and fragments and variants thereof.

The specification states that the polypeptide set forth as SEQ ID NO:2 is a motor protein of CENP-E 465 (pages 6 and 12, in particular). The specification further states that CENP-E is crucial for cell division (page 5, in particular).

The specification *prophetically* asserts a specific utility for polypeptides comprising SEQ ID NO:2 and fragments and variants thereof in methods of diagnosis, treatment and prevention of cancer, and neurological disorders (page 1, in particular). It is noted that the specification lacks working models using polypeptides comprising SEQ ID NO:2 and fragments and variants thereof to diagnose, treat, or prevent cancer or neurological disorders.

Following the requirements of the Utility Guidelines, (<http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf>), "substantial utility" is a utility that defines "real world use", wherein utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, the asserted "real world" utilities of the claimed polypeptides are use of said polypeptides in methods of diagnosis, treatment, and prevention of cancer and neurological disorders (see page 1, in particular). These asserted "real world" utilities are not supported by the specification or the prior art. The specification does not demonstrate that the claimed polypeptides are associated with any diseases or would predictably treat or detect any disease.

Further, in regards to using the claimed polypeptides to treat disease, treatments, in general, are unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of *In re* Brana (34 U.S.P.Q. 2d

1436, 1440 (Fed. Cir. 1995)). A review of *In re Brana* reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, the claims are not drawn to a polypeptide which has known in vivo ability to give rise to a therapeutic effect. Further, the instant specification provides no in vivo data, particularly demonstrating that the claimed polypeptide would predictably give rise to a therapeutic effect in vivo. In view of *In re Brana*, Examiner asserts that successful use of in vivo mouse models of specific diseases could demonstrate utility in humans and does not require human clinical testing; however, the instant application is claiming a polypeptide that provides a therapeutic effect without providing any in vivo data, hence the claimed invention is lacks utility. All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art, such as cancer and neurological therapeutics.

Further, in regards to using the claimed polypeptides to detect or diagnose, the state of the prior art dictates that if a molecule such as the claimed polypeptides to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a

cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the polypeptide's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the polypeptide in any diagnostic setting without undue experimentation.

Utility must be in readily available form. One of skill in the art would recognize that novel biological molecules, such as the claimed polypeptides, lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility. It is possible that, after further characterization, the claimed polypeptides or the antibodies that specifically bind the claimed polypeptides might be found to have patentable utility. This further characterization, however, is part of the act of the invention, and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.

The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where *specific* benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to polypeptides with undetermined biological significance. Until a specific real world utility is attributed to the claimed polypeptides, the claimed invention is incomplete. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptides. Because the claimed invention is not supported by a specific and substantial utility for the reasons set forth, credibility of any utility cannot be assessed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility and a substantial utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know *how to use* the claimed invention.

Claims 1, 3, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of: (1) a genus of polypeptides comprising "an" amino acid sequence as set forth in SEQ ID NO:2 (see claim 1); (2) a genus of polypeptides comprising "an" amino

acid sequence as set forth in SEQ ID NO:2, wherein said polypeptides comprise an amino acid sequence comprising "amino acids" at position 1 through 340 of SEQ ID NO:2 (see claim 19). However, the written description in this case only sets forth of polypeptides comprising the amino acid sequence as set forth in SEQ ID NO:2 and polypeptides comprising an amino acid sequence comprising the amino acid residues 1 to amino acid residues 340 of SEQ ID NO:2.

The state of the art is such Giot et al (US Patent 6753314; filed 3/29/00) teaches a sequence that comprises a 340 base pair sequence that is greater 99.7% identical to a sequence comprising the first 340 peptides of instant SEQ ID NO:2; however, said sequence is not representative of the broad genera of variants encompassed by the claims.

It is noted that a genus of polypeptides comprising "an" amino acid sequence as set forth in SEQ ID NO:2 is broadly drawn to any amino acid sequence *variant* sharing as few as two consecutive peptides of SEQ ID NO:2. It is further noted that a genus of polypeptides comprising "an" amino acid sequence as set forth in SEQ ID NO:2, wherein said polypeptides comprise an amino acid sequence comprising "amino acids" at position 1 through 340 of SEQ ID NO:2 is broadly drawn to any amino acid sequence variant sharing as few as two consecutive peptides and just any peptide found in position 1 through 340 of SEQ ID NO:2. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119

F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genera. That is, the specification provides neither a representative number of sequences that encompass the genera nor does it provide a description of structural features that are common to the genera. Further, in regards to genera encompassing variants, Applicant is directed to Example 13 of the Synopsis of Application of Written Description Guidelines (http://www.uspto.gov/web/menu/written.pdf), which addresses claims drawn to a genus of polypeptide variants. Example 13 states that even when a specification discloses that changes which produce variants are routinely done in the art, the specification and the claims do not provide any guidance as to precisely what changes should be made. Structural features that could distinguish the compounds of the claimed genera from others not encompassed by the genera are missing from the disclosure. No common structural attributes identify the members of the genera. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not

general, guidance is needed. Since the disclosure fails to describe common attributes or characteristics that identify members of the genera, and because the genera is highly variant, the disclosure of SEQ ID NO:12 is insufficient to describe the genera. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genera as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genera, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification

provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 18, and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Giot et al (US Patent 6,753,314; filed 3/29/00).

Giot et al teaches a polypeptide, SEQ ID NO:1252, which comprises a sequence that shares over 93.5% homology with the first 409 amino acids and greater than 99% homology with the first 340 amino acids of instant SEQ ID NO:2 (see attached sequence comparisons). It is further noted that SEQ ID NO:1252 and instant SEQ ID NO:2 share regions of 100% homology and comprises "an" amino acid sequence comprising many amino acids found at position 1 through 340 of instant SEQ ID NO:2. Thus, the purified polypeptide set forth in SEQ ID NO:1252 taught by Giot et al comprises "an" amino acid sequence as set forth in instant SEQ ID NO:2. Giot et al

further teaches a composition comprising the polypeptide set forth in SEQ ID NO:2 and a pharmaceutically acceptable excipient (see column 117, in particular).

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600